

**AMENDMENTS TO THE CLAIMS**

1-84. (Canceled).

85. (Previously Presented) A complex peptide mixture, comprising a plurality of peptides having a length within the range of 8 to 20 amino acids, wherein said mixture comprises peptides having a degree of diversity at defined positions in the peptide chain, wherein the degree of diversity in at least one defined position is different from the degree of diversity in at least one other defined position, and wherein in a majority of the mixture, the peptides include in at least four positions all of A, E, K, and Y and no other amino acids.

86. (Previously Presented) The peptide mixture of Claim 85, wherein in at least one position, a majority of the peptides in the mixture include each of one or two amino acids and no other amino acids.

87. (Previously Presented) The peptide mixture of Claim 85, wherein the amino acids in said at least four positions include all of A, E, K, and Y and no other amino acids in at least 75% of the peptides in the mixture.

88. (Previously Presented) The peptide mixture of Claim 85, wherein the amino acids in said at least four positions include all of A, E, K, and Y and no other amino acids in at least 90% of the peptides in the mixture.

89. (Previously Presented) The peptide mixture of Claim 85, wherein the amino acids in said at least four positions include all of A, E, K, and Y and no other amino acids in at least 95% of the peptides in the mixture.

90. (Previously Presented) The peptide mixture of Claim 85, wherein the amino acids in said at least four positions include all of A, E, K, and Y and no other amino acids in substantially all of the peptides in the mixture.

91. (Previously Presented) The peptide mixture of Claim 85, wherein a majority of the peptides in the mixture are acetylated at the N-terminal amino acid.

92. (Previously Presented) The peptide mixture of Claim 85, wherein the amino acids A, E, K, and Y in said at least four positions are present in the following molar proportions: about 6: about 2: about 5: about 1.

93. (Previously Presented) The peptide mixture of Claim 85, wherein in at least one position, a majority of the mixture consists of peptides that include all of I, L, and V and no other amino acids.

94. (Previously Presented) The peptide mixture of Claim 85, wherein in at least one position, a majority of the mixture consists of peptides that include all of H, R, and K and no other amino acids.

95. (Previously Presented) The peptide mixture of Claim 85, wherein in at least one position, a majority of the mixture consists of peptides that include all of K, H, R, and V and no other amino acids.

96. (Previously Presented) A complex peptide mixture, comprising a plurality of peptides having a length within the range of 8 to 20 amino acids, wherein said mixture comprises peptides having a degree of diversity at defined positions in the peptide chain and wherein at least in a majority of the mixture, the amino acids in the peptides include all of the following specified amino acids and no other amino acids:

- in at least four positions: A, E, K, and Y;
- in at least one position: I, L, and V;
- in at least one position: H, R, and K; and
- in at least one position: P and I.

97. (Previously Presented) The peptide mixture of Claim 96, wherein position P1 is the N-terminal residue.

98. (Previously Presented) The peptide mixture of Claim 96, wherein the N-terminal residue is acetylated.

99. (Previously Presented) The peptide mixture of Claim 96, wherein A, E, K, and Y are present in at least four of positions P1, P2, P3, P4, P6, and (if present), P9.

100. (Previously Presented) The peptide mixture of Claim 96, wherein said peptides have a length of at least 10 amino acids and A, E, K, and Y are present in all of positions P1, P2, P3, P4, P6, and P9.

101. (Previously Presented) The peptide mixture of Claim 96, wherein at least in a majority of the mixture, the amino acids at the carboxy terminus of the peptides include both P and I and no other amino acids.

102. (Previously Presented) The peptide mixture of Claim 96, wherein a majority of the peptides in the mixture have, in at least one position, the same amino acid.

103. (Previously Presented) A method of treating a disease, comprising administering to a vertebrate a complex peptide mixture, wherein said mixture comprises peptides having a constrained degree of diversity at each of at least 4 defined positions in the peptide chain and wherein the constrained degree of diversity in at least one defined position is different from the constrained degree of diversity in at least one other defined position.

104. (Previously Presented) The method of Claim 103, wherein said disease is selected from the group consisting of multiple sclerosis and experimental autoimmune encephalomyelitis.

105. (Previously Presented) A method for stimulating an immune cell comprising administration of a complex peptide mixture to said cell, wherein said mixture comprises peptides having a constrained degree of diversity at each of at least 4 defined positions in the peptide chain, and wherein the degree of diversity in at least one defined position is different from the degree of diversity in at least one other defined position.

106. (Previously Presented) The method of Claim 105, wherein said stimulating of an immune cell occurs in vivo.

107. (Previously Presented) The method of Claim 105, wherein said administering step is selected from the group consisting of intravenous delivery, intramuscular delivery, delivery via the gastrointestinal tract, and transdermal delivery.

108. (Previously Presented) A method for suppression of an immune reaction to an antigen, comprising administering a complex peptide mixture to an individual, said complex peptide mixture comprising peptides having a constrained degree of diversity at each of at least 10 defined positions in the peptide chain, and wherein the degree of diversity in at least one or two defined positions is different from the degree of diversity in at least one or two other defined positions.

109. (Previously Presented) The method of Claim 108, wherein said immune reaction is an autoimmune reaction.

110. (Previously Presented) The method of Claim 109, wherein said antigen is derived from myelin.

111. (Previously Presented) The method of Claim 108, wherein said peptide complex mixture comprises peptides of a defined length and formula comprising at least one position with a specific amino acid and at least one position with two to six possible amino acids.

112. (Previously Presented) The method of Claim 108, wherein said peptide complex mixture is a less-diverse subset of a complex mixture having a higher degree of diversity.

113. (Previously Presented) The method of Claim 108, wherein said complex mixture with a higher degree of diversity is a mixture whose formula is selected from the group consisting of the formulas listed in Table 1.

114. (Previously Presented) The method of Claim 108, wherein the activity of said peptide complex mixture is evaluated by an assay selected from the group consisting of a proliferation assay, a cytokine assay and a  $^{51}\text{Cr}$  release assay.

115. (Previously Presented) The method of Claim 110, wherein said suppression of an autoimmune reaction to myelin proteins is due to a mechanism selected from the group consisting of MHC blockade, TCR antagonism, tolerance induction, immune deviation/bystander suppression and cross reactivity with an antigen derived from a protein expressed within the central nervous system.

116. (Previously Presented) The method of Claim 110, wherein said myelin antigen is derived from a protein selected from the group consisting of myelin basic protein, proteolipid protein and myelin oligodendrocyte glycoprotein.

117. (Previously Presented) The method of Claim 108, wherein said antigen is derived from a protein expressed by a cell found in the central nervous system.

118. (Previously Presented) A method for inducing an anti-inflammatory response from immune system cells comprising administering a complex peptide mixture to immune system cells, said complex peptide mixture comprising peptides having a constrained degree of diversity at each of at least 10 defined positions in the peptide chain, and wherein the constrained degree of diversity in at least one or two said defined positions is different from the degree of diversity in at least another defined position.

119. (Previously Presented) The method of Claim 118, wherein said anti-inflammatory response comprises an alteration in immune cell activity selected from the group consisting of an upregulation of Th2/Th3 cell activity and a downregulation of Th1 cell activity.

**Application No.: 10/587,987**  
**Filing Date: December 2, 2008**

120. (Previously Presented) The method of Claim 118, wherein said anti-inflammatory response comprises an increase in the release of cytokines by cells, said cytokines selected from the group consisting of IL-4, IL-5, IL-10, TGF-beta and IL-13.

121. (Previously Presented) A method for creating a high affinity peptide ligand of a defined formula for a receptor of a T cell that is reactive to a myelin antigen, copolymer or an active mixture, comprising the deconvolution of a complex peptide mixture of a formula selected from the group consisting of the formulas listed in Table 1.

122. (Previously Presented) A complex peptide mixture, wherein said mixture comprises peptides between 4 and 100 amino acid residues in length, wherein said mixture has a constrained degree of diversity at each of at least 10 defined positions in the peptide chain, and wherein the degree of diversity in at least one defined position is different from the degree of diversity in at least one other defined position.

123. (Previously Presented) The complex peptide mixture of Claim 122, wherein the constrained degree of diversity is created by limiting the possible amino acids at each of the said defined positions to a list of possible amino acids that includes less than 10 amino acids.

124. (Previously Presented) The complex peptide mixture of Claim 123, wherein the list of possible amino acids for at least two of the said defined positions includes only 1, 2, or 3 amino acids.

125. (Previously Presented) The complex peptide mixture of Claim 122, wherein a majority of the peptides in the mixture have a length between about 4 and about 30 amino acid residues.

126. (Previously Presented) The complex peptide mixture of Claim 122, , wherein a majority of the peptides in the mixture vary in length by no more than 4 amino acid residues.

127. (Previously Presented) The complex mixture of Claim 122, wherein a majority of the peptides in the mixture are acetylated.

128. (Previously Presented) The complex mixture of Claim 122, wherein at least one position of one peptide in the mixture is occupied by a D-amino acid.

129. (Previously Presented) A method of enhancing a biological property of a complex mixture of peptides, peptidomimetics, or peptides and peptidomimetics, comprising:

providing a set of complex mixtures of reduced complexity that have a reduced degree of diversity from said complex mixture at least at one position;

testing each of said complex mixtures of reduced complexity and said complex mixture in an assay;

identifying complex mixtures of reduced complexity that have a greater or lesser activity in said assay than said complex mixture; and

enhancing the biological property of said complex mixture by incorporating the complexity-reducing features of at least one of said complex mixtures of reduced complexity that have greater or lesser activity in said assay than said complex mixture into the formula of said complex peptide mixture.

130. (Previously Presented) The method of Claim 129, wherein said biological property is selected from the group consisting of the ability to stimulate an immune system activity and the ability to suppress an immune system activity.

131. (Previously Presented) The method of Claim 130, wherein said immune system activity is selected from the group consisting of the clonal expansion of an immune system cell, the differentiation of an immune system cell, the activation of an immune system cell, the creation of an anergic state in an immune system cell, the creation of a memory immune cell population and the secretion of cytokines from an immune system cell.

132. (Previously Presented) The method of Claim 129, wherein said complex mixtures of reduced complexity comprise mixtures where the identity of the residue or amino acid in one or more positions in the mixture formula is limited to one functionality or amino acid.

133. (Previously Presented) The method of Claim 129, wherein said complex mixtures of reduced complexity comprise mixtures wherein the identity of the residue or amino acid in one or more positions in the mixture formula is limited to a formula less diverse than the formula for that position in said complex mixture of peptides, peptidomimetics, or peptides and peptidomimetics.

134. (Previously Presented) The method of Claim 129, wherein said assay is selected from the group consisting of an *in vitro* assay of peptide, peptidomimetic, or peptides and peptidomimetics recognition by an immune cell population and an assay of the effects of mixture administration on an organism.

**Application No.: 10/587,987**  
**Filing Date: December 2, 2008**

135. (Previously Presented) The method of Claim 134, wherein said assay of the effects of mixture administration on an organism is an assay of disease progression in the EAE mouse model.

136. (Previously Presented) The method of Claim 129, wherein enhancing the biological activity of said complex mixture of peptides, peptidomimetics, or peptides and peptidomimetics comprises the limiting of the identity of the amino acid or residue at a position in the compound formula to a single amino acid or functionality.

137. (Previously Presented) The method of Claim 129, wherein said biological property is the response measured in an in vivo model of disease.

138. (Previously Presented) The method of Claim 137, wherein said in vivo model is selected from the group comprising a model of anxiety, depression, obesity, cognition, neurological disorder, motor disorder, or pain.

139. (Currently Amended) A complex peptide mixture, comprising a plurality of peptides having a length within the range of 8 to 20 amino acids, wherein said mixture comprises peptides having a degree of diversity at defined positions in the peptide chain, and wherein at least in a majority of the mixture, the identity of 10 contiguous amino acids in the peptides are defined by the following formulas: FW-EF-EK-AEK-AKY-ANY-ANY-AINV-ASV-Y (SEQ ID NO: 1); or EFWY-EFIVWY-EFKQ-AEKQ-AKQY-ANQY-AGNSY-AGINSV-AIQSV-IKRSVY (SEQ ID NO: 2).

140. (Previously Presented) The peptide mixture of Claim 139, wherein position P1 of the 9 contiguous amino acid residues is the N-terminal peptide.

141. (Previously Presented) A complex peptide mixture, comprising a plurality of peptides having a length within the range of 8 to 20 amino acids, wherein said mixture comprises peptides having a degree of diversity at defined positions in the peptide chain, wherein the degree of diversity in at least one defined position is different from the degree of diversity in at least one other defined position, wherein in a majority of the mixture, the peptides include in at least one but no more than five positions all of A, E, K, and Y and no other amino acids.